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EXAMINER	
NOAKES, SUZANNE MARIE	
ART UNIT	PAPER NUMBER
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,098	PETZELT, CHRISTIAN	
	Examiner	Art Unit	
	Suzanne M. Noakes, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 7-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 July 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-29-2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions – Lack of Unity

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-5, 7 and 8, drawn to an isolated nucleic acid encoding the protein cysplasin which lacks a function or has no secretory signal sequence of SEQ ID No: 1 (20 or 53 to 558) or SEQ ID No: 5 and derivatives thereof.

Group II, claims 6, 12 and 13, drawn to an isolated protein encoded by a nucleic acid encoding the protein cysplasin which lacks a function or has no secretory signal sequence of SEQ ID No: 1 (20 or 53 to 558) or SEQ ID No: 5 and pharmaceutical compositions thereof.

Group III, claims 10 and 11, drawn to a pharmaceutical composition comprising a nucleic acid encoding the protein cysplasin which lacks a function or has no secretory signal sequence of SEQ ID No: 1 (20 or 53 to 558) or SEQ ID No: 5 and derivatives thereof.

2. The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Claim 6, is drawn to an isolated protein encoded by a nucleic acid molecule wherein said nucleic acid encodes: (a) a polypeptide of 20-558 or 53-558 of SEQ ID No: 1, (b) wherein the nucleic acid is SEQ ID No: 5 (which encodes 53-558 of SEQ ID No: 1), (c) wherein the nucleic acid is a derivative due to the degeneracy of the genetic code, or (d) wherein the nucleic acid is a fragment, derivative or allelic variant of a-c. A derivative is defined in the

specification as being 40, 60, 70, 80, 85, 90, 92, 95, 97, 98 or 99% sequence identity (see p. 9, last paragraph). Takamatsu et al. (FEBS Lett., 1995, 377:373-76) teach a protein isolated from *Aplysia kurodai* which is 556 amino acids in length and which said protein exhibits antimicrobial activity and lyses tumor cells (see p. 373, Abstract, and 1st column, 4th sentence from bottom). Said protein is 73.9% identical to amino acids 20-558 of the instant SEQ ID No: 1 (see Appendix A and/or results in SCORE) and is thus a derivative thereof which at the minimum meets the limitations of claim 6(d).

Therefore, the technical feature linking the inventions of Groups I-III does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not differentiate the claimed subject matter as a whole over the prior art. Since according to PCT Rule 13.2 the presence of such a common or corresponding special technical feature is an absolute prerequisite for unity to be established, and given that there does not appear to be any other technical feature common to the claimed subject matter as a whole which might be able to fulfill this role, the currently claimed subject matter lacks unity of invention according to PCT Rule 13.1.

3. A telephone call was made to Mr. Stephen Hultquist on September 05 2006 to request an oral election to the above restriction requirement, but did not result in an immediate election being made. However, Mr. Hultquist instead responded in writing on 06 October 2006 and elected Group II, claims 6, 12 and 13. A preliminary amendment to the claims was simultaneously submitted which added claims 14 and 15. Claims 14 and 15 are read upon the elected invention.

Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-5, 7, 8, 10 and 11 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Status of the Application

4. Applicants have added two claims, 14 and 15 by way of preliminary amendment on 06 October 2006. Claims 1-15 are pending and claims 1-5 and 7-11 are withdrawn from further consideration as stated above. Claims 6 and 12-15 are subject to examination.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 29 November 2004 has been considered by the examiner. See initialed and signed PTO-1449.

Drawings

6. The drawings are objected to under 37 CFR 1.83(a) because they fail to show the details as described in the specification. Specifically, Figures 4, 7-9 and 12 are of insufficient quality to be able to differentiate the details which are described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing

sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Compliance with Sequence Rules

7. The sequence listing, filed in computer readable form (CRF) and paper copy on July 7, 2002, has been received and entered. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

A. The following Figures contain sequences without any SEQ ID NO: and/or no reference to any SEQ ID NO: in the Brief Description of the Drawings.

i) Figure 2(a) is a sequence alignment between cyplasin-L (upper sequence) and cyplasin-S (lower sequence).

ii) Figure 2(b) is a DNA sequence of Cyp1-(Mut)-(-Sig. Seq).

iii) Figure 10 shows a sequence which is described as the likely signal peptide sequence and its cleavage site(s).

iv) Figure 11 is an amino acid sequence of cyplasin with the secretory leader sequence removed.

An amendment to either the drawing or to the description of said drawing will rectify the situation.

B. In the specification, pp. 21 (last paragraph) and p. 25 (last paragraph) of the specification contain sequences of four or more amino acids without any SEQ ID No: identifier (see MPEP 2421.02).

* If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Specification

8. The disclosure is objected to because of the following informalities:

A. It is suggested that "Aplysia punctata" as recited in the title be italicized to reflect the accepted genus-species identifier.

B. On page 3, the heading identifier for the Figures is labeled as "Figure legends". 37 CFR 1.77(b) requires that each section heading should appear in upper case, without underlining or bold type. Thus, it is suggested that this section heading be changed to "BRIEF DESCRIPTION OF THE DRAWINGS".

C. The description of Figure 4 on page 4-5 of specification describes Figures (a), (b) and (c); however, there is no (a), (b) or (c) labeled in the drawing. It appears Applicants are referring to the lanes of the SDS-page gel and thus it is suggested that Applicants might simply wish to refer to the lanes as being left, middle and right so as to avoid confusion.

Appropriate corrections are required.

Claim Objections

9. Claim 6 is objected to because of the following informalities: In part c) of claim 6, it is suggested to add a comma between 'a nucleic acid molecule' and 'the nucleic acid sequence.....', so the claim is more clear. Appropriate correction is required.

Claim Rejections - 35 USC § 112 – 1st paragraph

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description:

11. Claim 6 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claim 6, part (d), is drawn to an isolated protein that it encoded by a nucleic acid molecule wherein the nucleic acid encodes a fragment, derivative or allelic variant of: a) SEQ ID No: 1 (amino acids 20-588 or 53-588), b) SEQ ID No: 5 or c) wherein the DNA encoding said proteins a) and b) deviates due to the degeneracy of the genetic code. The specification defines fragments, deviations and allelic variants as follows: a) fragments are to be parts of the nucleic acid molecule that are long enough to encode one of the described proteins (see p. 9, 2nd paragraph); derivatives are defined as sequences that differ from the defined sequences by 40, 60, 70, 80, 85, 90, 92, 95, 97, 98 or 99% sequence identity (see p. 9, last paragraph) wherein said deviations are produced by deletion, substitution, insertion or recombination; and allelic variants are defined as naturally occurring or synthetically produced variants or variants produced by recombinant DNA processes (see p. 10, 1st paragraph, last line). Thus, the claim and those that depend therefrom are drawn to a large genus containing thousands of potential DNA sequences/species.

The MPEP states that written description for a genus can be achieved by a representative number of species and that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Thus, to satisfy the written description aspect of 35 U.S.C. 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

In the instant case there are three species defined in the specification which fall within the scope of the genus. The full length nucleic acid that encodes all of SEQ ID No: 1 or the nucleic acid sequences which encode amino acids 20-588 or 53-588 of SEQ ID No: 1 or SEQ ID No: 5 (which is DNA molecule that encodes a 506 amino acid cyplasin protein – wherein said protein lacks the first 52 amino acids of SEQ ID No: 1). However, there are numerous other species which may be fragments thereof of these species, or which may have anywhere from 40, 60, 70, 80, 85, 90, 92, 95, 97, 98 or 99% identity of said species or which may be naturally occurring, synthetic or recombinantly produced allelic variants, all of which is tantamount to any kind of variation. Furthermore, none of the fragments, derivatives or allelic variants are required to have any sort of function or activity. In addition, there is no description of

the mutational sites that exist in nature and there is no description of how the proteins encoded by SEQ ID NO: 1 or the protein which is encoded by SEQ ID No: 5 are related to the structure of the different encoded fragments, derivatives or alleles. For instance, which amino acids are essential for the protein cytotoxicity or which proteins are essential to the folding of said proteins (and also thus function), etc. The general knowledge in the art concerning fragments, derivatives or alleles does not provide any indication of how the structure of the wild-type proteins or proteins lacking signal peptides are representative of other unknown fragments, derivatives or alleles having concordant or discordant functions. Furthermore, the prior art is of little assistance because this is a novel protein which has not been assigned to any particular protein or enzymatic family. Applicants do show that cyplasin-L has several amino acids in common with monoamine oxidases but none appear to be essential active site residues (See Figs. 1-3 and 7, Edmondson et al. Curr. Med. Chem., 2004, 11:1983-93). Furthermore, it can not be concluded that this protein is a member of this class of proteins without verifying the existence of a FAD co-factor and/or activity. The common attributes of the genus are not described and the identifying attributes of individual fragments, derivatives or alleles, other than the nucleic acid encoding SEQ ID NO:1, amino acids 20-588, 53-588 or SEQ ID No: 5 are not described. The nature of any or all fragments, derivatives and alleles is that they have variant structures where the structure and function of one does not provide necessarily provide guidance to the structure and function of others.

It should be noted, the description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). *Vas-Cath Inc. V. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed."* Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim. Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Scope of Enablement:

12. Claims 6 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated protein encoded by a nucleic acid

that is amino acid 20-588 or 53-588 of SEQ ID No: 1, is SEQ ID No: 5 or which said nucleic acids deviate due to the degeneracy of the genetic code but encode the same protein, does not reasonably provide enablement for fragments, derivatives or allelic variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 6, part (d), is drawn to an isolated protein that it encoded by a nucleic acid molecule wherein the nucleic acid encodes a fragment, derivative or allelic variant of: a) SEQ ID No: 1 (amino acids 20-588 or 53-588), b) SEQ ID No: 5 or c) wherein the DNA encoding said proteins a) and b) deviates due to the degeneracy of the genetic code d) fragments, derivatives or allelic variants thereof. The definition of each (d) is described in the specification on pp. 9-10 and in preceding Section 11. The specification discloses an isolated protein cyplasin-L, consisting of SEQ ID No: 1, with and without a functional signal peptide (e.g. amino acids 20-588 or 53-588 of SEQ ID No: 1). The specification further establishes that this protein has cytotoxic activity and provides an assay for this activity. General guidance is given regarding how to make and test variants of the proteins by hybridization ability. However, the scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons. The problem of prediction protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in

any given protein, the positions within the protein's sequence where such amino acid substitutions, insertions, deletions, etc. can be made with a reasonable expectation of success is limited. Certain positions in the sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity and/or in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions as all (see Bowie et al. Science, 1990, 247:1306-10, specifically p. 1306 column 2, paragraph 2; Wells, Biochemistry, 1990, 29(37), pp. 8509-17). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. by amino acid substitutions or deletions or insertions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active protein variants, this is not adequate guidance as to the nature of active fragments, derivatives or allelic variants that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, this may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which said conformation is dependent upon the

surrounding residues; therefore substitution of non-essential residues can often destroy activity or prevent folding.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen the same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which established the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 6, 12, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Takamatsu et al. (FEBS Lett., 1995, 377:373-76) as evidenced by Kamiya et al. (Experientia, 1986, 42:1065-67).

The teachings of Takamatsu et al. are described above in Section 2 of this Office action. In summary, Takamatsu et al. teach a 556 amino acid protein with anti-tumor

and anti-microbial activity isolated from a cDNA clone, which is 73.9% identical to amino acids 20-558 of SEQ ID No: 1 (see sequence alignment or the results which are publicly available in SCORE). Thus, said protein is a derivative of SEQ ID No: 1 and meets the limitations of claim 6(d). In addition, the protein isolated by Takamatsu et al. was isolated 'as previously described' which refers to the isolation of the protein from its original source (*Aplysia kurodai*) described and evidenced by Kamiya et al. Kamiya et al. reports isolating the protein in a pharmaceutically acceptable buffer wherein the active fractions were eluted from a DEAE column in a 10mM phosphate buffer at pH 7.4 and had a final salt concentration of up to 200 mM NaCl (seep. 1066, 2nd column). Thus, the protein reported by Takamatsu et al. was purified in the same way and in the same pharmaceutically acceptable buffer.

While Takamatsu et al. do teach that their isolated protein does have anti-tumor activity, the intended use recited claim 13 is not given any patentable weight in the instant situation because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, as is the case here, then it meets the claim. See *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

The limitations recited in claim 15 are limited to a protein which only has to exhibit biological properties like cyplasin, however, the claim does not require that the protein *is* cyplasin. As such, the protein described by Takamatsu et al., which is a

protein that exhibits anti-microbial and anti-tumor activity and which does exhibit biological properties like cyplasin and thus the limitations of the claim have been met.

15. Claims 6 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Petzelt (NCBI database accession AJ304802 – cited on the IDS of 11/29/04).

Petzelt teaches a deposit from *Aplysia punctata*, mRNA for cyplasin-L and its deduced amino acid sequence. Said amino acid sequence is 100% identical to the instant SEQ ID No: 1 (see Appendix B or results in SCORE). Claim 6 recites an isolated protein encoded by a nucleic acid molecule which encodes: (a) a protein *comprising* the amino acid sequence from 20-558 or 53-558 or (b) a nucleic acid molecule *comprising* the sequence of SEQ ID No: 5, or derivatives thereof (d). Thus, the protein disclosed by Petzelt on 18 December 2000 anticipates the instant claim 6. Since Petzelt discloses that the deposit *is* cyplasin-L then inherently said protein will necessarily exhibit biological properties consistent with its natural/innate biological function.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petzelt (Accesion AJ304802 – cited on IDS) and in view of Yamazaki (Comp. Biochem. Physiol C. 1993,105(2):141-6) and Petzelt (US 6,171,818).

The teaching of Petzelt's deposit is recited in Section 15 of this Office action. Furthermore, the notes of the deposit state that Cyplasin-L is a cytolytic protein from the sea hare *Aplysia punctata* (see under heading [2] - Title). Said deposit, however, does not teach or suggest putting said protein in a pharmaceutical composition.

Yamazaki teaches that many novel antitumor and antimicrobial gylycoproteins have been isolated from *Aplysia kurodai, Aplysia juliana* and *Dolabella auricularia* and that all proteins that have been identified and isolated thus far, lyse tumor cells. It was thus suggested that sea hares might produce water-soluble gene-expressed biopolymers/protein of pharmacological interest. Yamazaki, however, does not teach cyplasin or any other proteins from *Aplysia punctata* and/or suggest to put these into a pharmaceutical composition.

Petzelt '818 teaches a protein isolated from *Aplysia punctata* which has antitumor activity (see column 1, lines 20-32). Petzelt '818, however, does not teach any protein of the instant claim 6 in a pharmaceutical composition.

Nonetheless, given that the protein identified by the Petzelt's deposit is a cytolytic protein from sea hares, and that Yamazaki suggested that sea hares produce many proteins which possess pharmacological properties, and furthermore that Petzelt '818 identified the existence of some of these antitumor pharmacological proteins in the same species that the Petzelt deposit is isolated from, *Aplysia punctata*, then it

therefore would have been obvious to one of ordinary skill in the art at the time the invention was made to place the Petzelt protein deposited as Accession AJ304802 into a pharmaceutical composition. One of ordinary skill in the art would be motivated to place the deposited protein into a pharmaceutical compositions because it would be obvious to want to ascertain if the cytolytic protein of Petzelt (accession) also has antitumor pharmacological properties similar to those proteins identified from other sea hares as disclosed by Yamazaki. Thus, if one wants to use said protein for its pharmacological cytolytic properties then said protein would be required to be in a pharmaceutical composition for testing purposes (e.g. antitumor or antimicrobial testing). Furthermore, there would be a reasonable expectation of success in placing said protein into a pharmaceutical composition because this is a routine practice in the art. The intended use language for treating cancer with said pharmaceutical composition again is not given patentable because the intended use does not patentably distinguish the claimed invention from the prior art.

It should be noted that the motivation to combine said references, while not explicitly stated in said references, is derived from general knowledge as a whole in the prior art (e.g. sea hares produce a lot of pharmacologically relevant proteins with cytolytic antitumor activity and the instant protein has cytolytic activity – thus it is likely a pharmacologically relevant protein and it would hence be advantageous to place said protein in a pharmaceutical composition). The US Federal Circuit has recently explicitly stated that in order to make a *prima facie* case of obviousness, the suggestion and motivation to combine said references need not be explicitly stated in the text of the

references. Rather, common knowledge and common sense are not only permitted by required when performing an obviousness test. See DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co., 80 USPQ2d 1641 (Fed. Cir. 2006) which states:

> "Suggestion" test for obviousness does not require that suggestion, teaching, or motivation to combine cited prior art references be found in references themselves, or that such suggestion or motivation be explicitly stated; [the] suggestion test is flexible rather than rigid and categorical, recognizing motivation to combine found in [the] knowledge of persons of ordinary skill in art or nature of problem to be solved, as well as in references, and [the] test not only permits, but requires, consideration of common knowledge and common sense."

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make place Petzelt's deposited protein into a pharmaceutical composition for the reasons stated above.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suzanne M. Noakes, Ph.D. whose telephone number is 571-272-2924. The examiner can normally be reached on Monday to Friday, 7.00am to 3.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SMN
10 January 2007

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